PTO 2001-2959

Japanese Article
Kohno

DEVELOPMENT AND OF "SEBUM ANTIOXIDANT THIOTAURINE" FOR COSMETICS ITS APPLICATION

["Hishikohsankazai=chiotaurin" No Kaihatsu to Keshohin Heno Ouyo]

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UNITED STATES PATENT AND TRADEMARK OFFICE
Washington, D.C. June 2001

Translated by: Diplomatic Language Services, Inc.

TRANSLATED TITLE	:	DEVELOPMENT OF "SEBUM ANTIOXIDANT THIOTAURINE" FOR COSMETICS AND ITS APPLICATION
FOREIGN TITLE	:	"HISHIKOHSANKAZAI=CHIOTAURIN" NO KAIHATSU TO KESHOHIN HENO OUYO
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SOURCE	:	FRAGRANCE JOURNAL 1998-12, DECEMBER, 1998, PP. 9-14

Abstract: Cosmetics and quasi-drugs will play increasingly important roles in our aging and stressful society. We have proposed 3 clinical approaches, anti-drying, anti-UV radiation and anti-oxidation to prevent skin disorders and aging. In this paper the importance of anti-oxidation mechanisms in particular are discussed. We have discovered that sebum oxidation, which is the starting point of skin oxidation, is triggered by oxidation of squalene. Further research on antioxidant effects of natural ingredients revealed that thiotaurine is effective in preventing squalene oxidation, which leads to the prevention of further propagation of oxidation in the skin. Thiotaurine is known to be compounds involved the metabolism of sulfur-containing amino acids in mammals. We have clarified that thiotaurine in skin care products prevents sebum oxidation and consequently prevents skin troubles and skin aging.
Key words: thiotaurine, antioxidant, lipid peroxidation, sebum, singlet oxygen

/9*

1. Introduction:

Since 1989, Shiseido has been engaged in research and development work related to the theme "Successful aging, for living many beautiful years." This has been the backbone of the business culture. In our research and development department also, we intend to realize "successful aging" by making the products developed in our department available to consumers.

Skin, which is the human body's largest organ, is located at the boundary region which separates the living body from the outside world,

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*Numbers in the margin indicate pagination in the foreign text.

and is exposed to constant irritation and stress. As this exposure is repeated over many years, damage is accumulated in the skin, even though each individual damage may be small. Therefore, human skin is known as the organ where "age signs" easily appear, and its change with age has been concerning. Since skin is such a sensitive organ, proper skin-care is important in order to realize "successful aging."

As stresses from the outside environment causing skin disorders (e.g., rough skin, dry skin, pimples, rash and the like) and skin ageing (wrinkles, liver spots, freckles, dark spots, lowering of skin softness, slackness, lowering of immunological functions and the like), "drying," "ultraviolet ray exposure," and "oxidation" can be considered. The author, et al. have been emphasizing the importance of "defense against drying," "defense against ultraviolet rays" and "defense against oxidation" as the defense strategy from the viewpoint of skin-care needed to cope with skin disorder and skin aging (see Figure 1). Furthermore, it has been known that these three stresses are closely related. Ultraviolet rays are the factors contributing most to oxidation, and ultraviolet rays cause skin dryness. Furthermore, /10 oxidation causes skin dryness, and dried skin is easily oxidized.

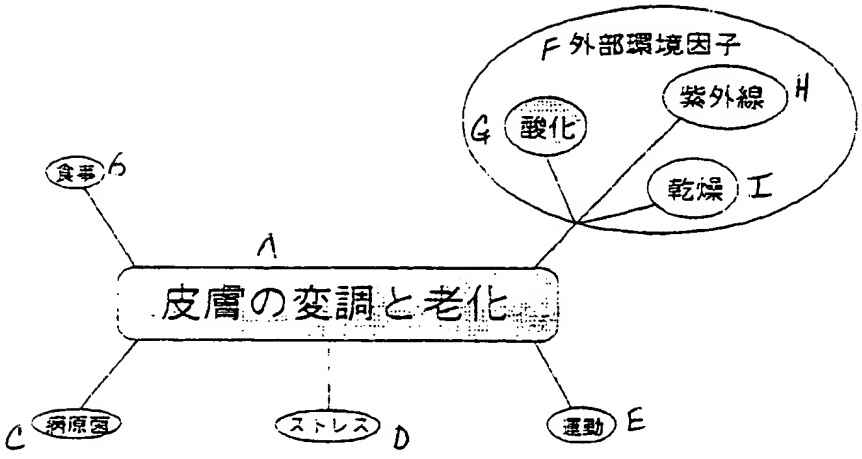

Figure 1
[Key:]
Skin disorders and aging and their causes

A...Skin disorders and aging; B...pathogens; C...meals; D...stress; E...exercise, sports; F...External environmental factors; G...oxidation H...ultraviolet rays; I...drying

In this paper, attention is paid to the "defense against oxidation," and examples of desired material development are introduced. Considering the "defense against oxidation" from the aspect of cosmetics compounding, an "antioxidant" is added only for the purpose of stabilizing those materials to be added to the cosmetics. Although it is obvious that it is important, from the viewpoint of the quality assurance and safety of cosmetics, to secure oxidation stability of the medicines and oils which are the constituents of cosmetics, materials which are clearly aimed as oxidation prevention in skin constituents are not developed thus far. The author, et al., in order to develop such

materials, have investigated the mechanism of oxidation of skin constituent lipids, and investigated the effects of peroxidation reaction on living body skin. Furthermore, the author, et al. also investigated the meaning of prevention against "skin oxidation" by cosmetics [1, 2]. In this report, the usability and function of "sebum antioxidant=thiotaurine," which was added to "ERIKSEAL [transliteration]," which was made commercially available in September 1998 for the purpose of maintaining healthy skin, are summarized.

2. Oxidation in skin:

In general, as new methodology is developed, progress is made in understanding of phenomena occurring in the natural world that is not clearly understood. By using the methodology, constituents which are effective in coping with the phenomenon can be found, which leads to development of new constituents and new products.

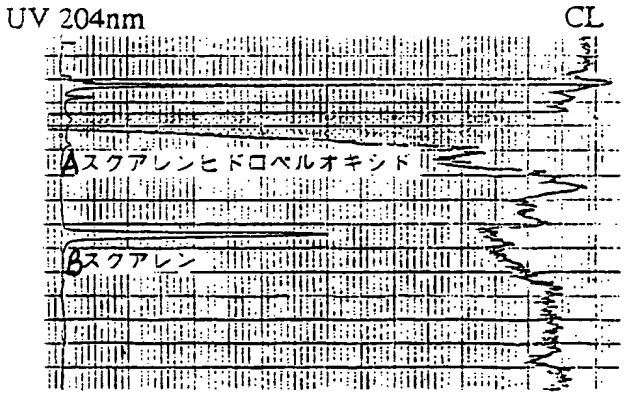

Figure 2
Oxidized sebum
(April, sunny weather, exposed to sun light for 30 minutes)

[Key:]
A...squalene hydroperoxide
B...squalene

Additionally, with thiotaurine, the CL-HPLC system [3, 4], which is a new methodology, has largely contributed to its development. Figure 2 shows a chromatogram with which a series of research activities conducted by the author and his associates were initiated. This chromatogram shows the results of a CL-HPLC analysis of sebum, which was collected from skin that was exposed to the sun light. The fully swinging chart gave a hint for development of new cosmetic materials which were not catagorized thus far. Thereafter, it was also reported [5-7] that in skin oxidation, squalene in sebum was oxidized first; squalene hydroperoxide was identified by spectrum analysis; and that the CL-HPLC system had detection sensitivity reaching to the order of /11 fmol. It was also reported that lipid peroxidation reaction at skin surface increased as the dosage of ultraviolet ray radiation on human increased (see Figure 3); and that, through the observation of the dependency of lipid peroxidation reactions at the human skin surface on age difference, the degree of peroxidation was higher in early childhood, during which the protective system is not fully developed, and at old age, during which the protective system is deteriorating (see Figure 4). In addition, the author, et al. also found that squalene hydroperoxide, which is always formed on the human skin surface by various kinds of oxidation stresses in general living environmental conditions, had cytotoxicity. Through an investigation using a skin restructuring system, which closely resembles the actual skin, it was found that fibroblast and Keratinocyte inside the skin were damaged by the oxidation propagation reaction of radicals generated from squalene hydroperoxide. In other words, the oxidation of sebum is the beginning

of oxidation in skin. It can be considered [8] that it is not only the phenomenon occurring simply on the skin, but also adversely affects the inside part of the skin.

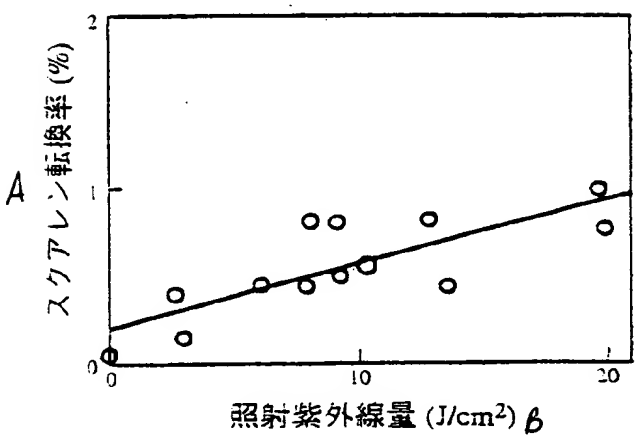

Figure 3
Lipid peroxidation reaction in human skin surface
(Effect of dosage of ultraviolet ray irradiation)

[Key:]
A...Squalene conversion ratio (%); B...Dosage of ultraviolet ray irradiation (J/cm^2)

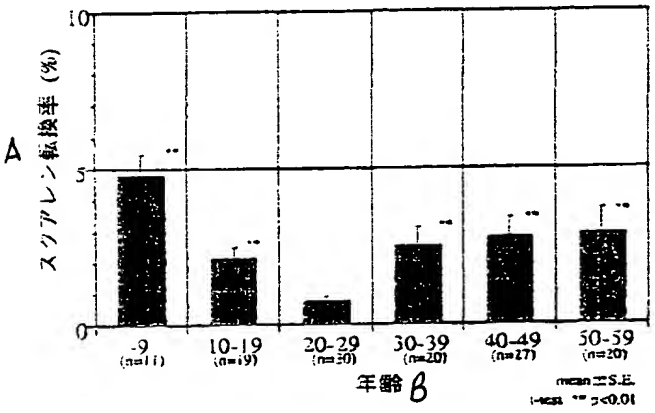

Figure 4
Lipid peroxidation reaction of human skin surface
(Effect of age)

[Key:]
A...Squalene conversion ratio (%); B...Age

TABLE 1
Singlet oxygen reaction rate constant (k_q) of lipids

	脂質類 A	化学式 B	二重結合数 C	kQ [$M^{-1}s^{-1}$]
D	オレイン酸	$C_{17}H_{33}COOH$	1	1.7×10^4
E	リノール酸	$C_{17}H_{31}COOH$	2	4.2×10^4
F	リノレン酸	$C_{17}H_{29}COOH$	3	8.0×10^4
G	アラキドン酸	$C_{19}H_{31}COOH$	4	10.0×10^4
H	ドコサヘキサエン酸	$C_{21}H_{31}COOH$	6	15.0×10^4
I	スクアレン	$C_{30}H_{50}$	6	56.2×10^5
J	コレステロール	$C_{27}H_{46}O$	1	6.7×10^4

[Key:]
A...Lipids; B...Chemical formula; C...Number of double bonds; D...oleic acid; E...linoleic acid; F...linolenic acid; G...arachidonic acid; H...docosahexaenic acid; I...squalene; J...cholesterol

3. Physicochemical understanding of oxidation reactions in skin:

Physicochemical observation was made of the phenomenon explained in the previous section [9]. Measurement of the reaction rate constant between lipids existing in skin and singlet oxygen indicated that squalene was reactive with singlet oxygen (see Table 1). Although singlet oxygen may also be generated in healthy human skin under general living environmental conditions, squalene can be the initial oxidation target at the human skin surface for the reasons described above. This fact provides a scientific basis which strongly hints that it is the active oxygen type in which singlet oxygen is the key element at skin surface. In other words, in order to design cosmetics for coping with skin oxidation, first of all, it can be considered necessary to cope with singlet oxygen. Furthermore, as a measurable parameter, it /12 is useful to monitor the degree of peroxidation of sebum.

4. Development of the sebum antioxidant "thiotaurine":

In order to prevent oxidation of the skin and to maintain healthy

skin, it is important to prevent sebum oxidation which is the first step of oxidation in skin. Specifically, materials having high singlet oxygen eliminating activity should be applied to the skin. In addition, it is necessary that the materials be not only superior in singlet oxygen eliminating activity, but also safe, easily compoundable, stably compoundable, and safe as commercial products. In other words, for the design and selection of cosmetics materials advocating antioxidation of skin constituents, it is important that they be totally balanced as cosmetics materials.

Based on the viewpoint described above, candidate materials were screened. We selected these materials from living body constituents. In order to maintain the balance of living body skin, it was planned to supply thiol compounds, which easily fluctuate by receiving oxidation stress, and to reinforce and restructure a living body defense system [10]. The thiotaurine selected by the author, et al., is also a material existing in sulfur-containing amino acid metabolic process in mammals (see Figure 5). Since these compounds exist in relatively large quantities in the eyes and generative organs, which are considered to be exposed to outside oxidation stress or to be consuming a large quantity of energy, there are reports discussing the theory that thiotaurine and hypotaurine exist in the metabolic process.

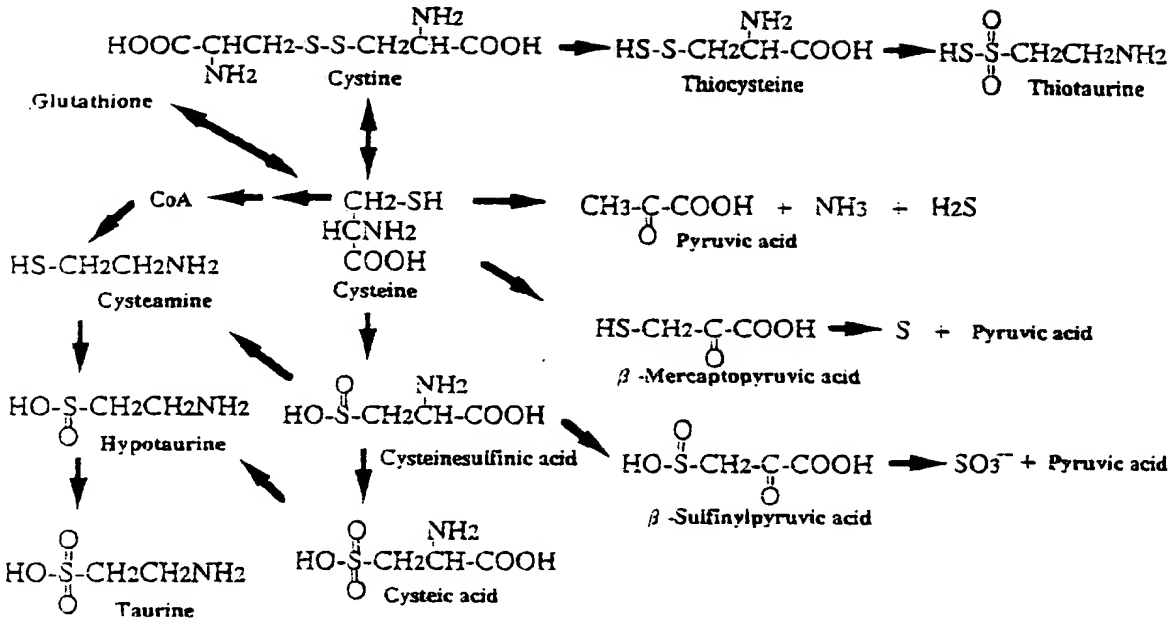

Figure 5
Metabolism of sulfur-containing amino acid
(A. White, P. Handler, E.L. Smith; Principles of Biochemistry)

5. Moisture retaining properties of thiotaurine:

In a broad sense, thiotaurine is a kind of amino acid, and could have a potential moisture retaining effect. The author, et al., verified the moisture-retaining effect on human skin as well as its durability (see Figure 6). It was confirmed that its moisture-retaining effect was not inferior compared to that of a typical moisture-retaining agent which is already in use. It was mentioned earlier that drying and oxidation are related. In order to maintain healthy skin, it is expected that a "defense against drying" and a "defense against oxidation" function synergistically.

6. Antioxidation properties of thiotaurine:

The rate constant of the singlet oxygen reaction of thiotaurine was measured, and the result is shown in Table 2. Thiotaurine had higher singlet oxygen eliminating activity compared to a typical antioxidant /13 which is also used in cosmetics. By considering the number of mols of squalene on human skin calculated from the sebum secretion quantity, and the number of mols of thiotaurine to be applied to skin as cosmetics, and also from the rates of reaction between singlet oxygen and squalene, and between singlet oxygen and thiotaurine respectively, how far the peroxidation reaction which occurs on the human skin surface can be prevented can be calculated. Since, physicochemically, the singlet oxygen eliminating activity of thiotaurine was more than sufficiently satisfactory, thiotaurine-containing cream was prepared, and was applied to the human skin surface to confirm its effect. In detail, the site where a cream containing a prescribed amount of thiotaurine was applied, the site where a cream containing no thiotaurine (other compositions were unchanged) was applied, and the site where no cream was applied were respectively set, and were radiated with ultraviolet rays. In addition, sebum samples were collected from the respective sites and were subjected to CL-HPLC analysis to obtain the proportions of peroxidized squalene. The result is shown in Figure 7. Compared to the blank site where no cream was applied and the placebo cream application site where a cream containing no thiotaurine was applied, sebum at the site where a cream containing thiotaurine was applied was statistically significantly prevented from oxidation. It was also confirmed that its effect depended on the compounding concentration of thiotaurine.

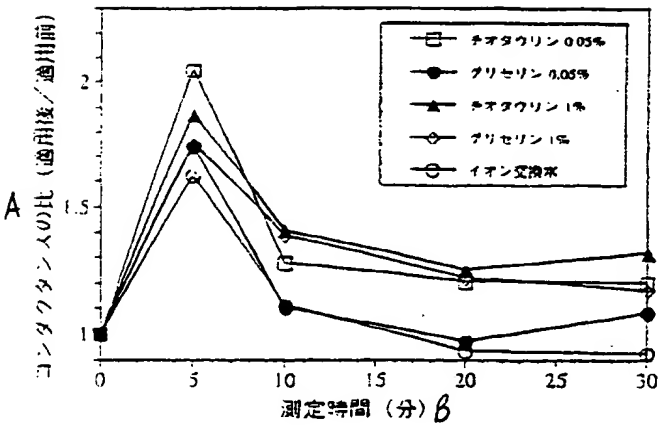

Figure 6
Comparison of moisture retaining effects of thiotaurine and glycerine (n=9)

[Key:]
A...Conductance ratio (after application/before application); B...Measurement time (min.); C...thiotaurine 0.05%; D...glycerine 0.05%; E...thiotaurine 1%; F...glycerine 1%; G...ion-exchanged water

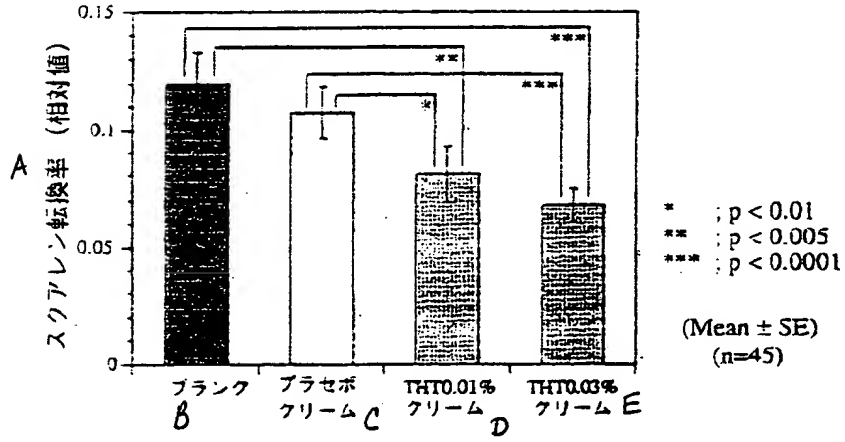

Figure 7
Human sebum oxidation prevention effect of thiotaurine THT: thiotaurine

[Key:]
A...Squalene conversion ratio (relative values); B...blank; C...placebo cream; D...THT 0.01% cream; E...THT 0.03% cream

TABLE 2
Singlet oxygen reaction rate constant (k_q) of antioxidant

Antioxidants	**k_Q [$M^{-1}s^{-1}$]**
thiotaurine	2.45×10^7
hypotaurine	6.97×10^6
BHT	4.91×10^6
d-α-tocopherol acetate	1.60×10^6
ascorbic acid	8.30×10^6
squalene	5.62×10^6

7. Stability of thiotaurine:

The stability of the thiotaurine that was mixed in cosmetics was also investigated. The result is shown in Figure 8. It was confirmed that thiotaurine was relatively stable against heat (50°C) or light (i.e., exposure to sun light). It is considered significantly unique among the compounds having an antioxidation effect. Furthermore, even /14
if it were oxidized and changed, the product is characterized by the fact that its main constituent is hypotaurine or taurine, which are already being approved as raw materials for cosmetics (i.e., its safety is assured). It also shows that, as a cosmetics material, thiotaurine is an antioxidant having an excellent total balance.

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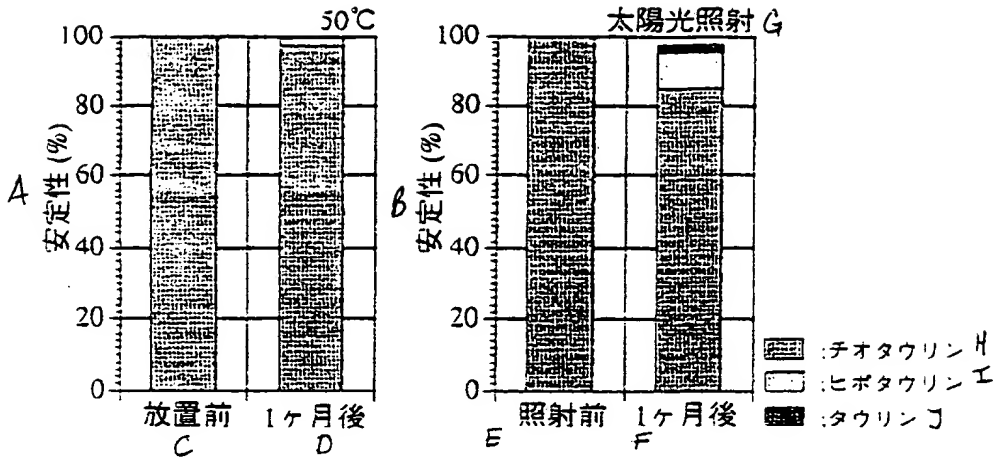

Figure 8
Stability of thiotaurine (pH=6.0)

[Key:]
A...Stability (%); B...Stability (%); C...before placement; D...one month later; E...before irradiation; F...one month later; G...sun light irradiation; H...thiotaurine; I...hypotaurine; J...taurine

8. Conclusion:

The author, et al., developed sebum antioxidant=thiotaurine as a cosmetics material. The effect of thiotaurine was verified on humans, and it was confirmed that its safety and stability are excellent. In other words, thiotaurine was excellent, as a whole, as an antioxidant for cosmetics. Physiologically speaking, the application of cosmetics in which thiotaurine is mixed is to prevent the first stage of skin oxidation; that is, to prevent oxidation of sebum, which can be said to be the first sign of aging in human beings. The author, et al., believe that it is important to age beautifully, and it is an important means for skin care with which "successful aging" can be realized.

CITED LITERATURE

1. Kohno, Y.Y., and Takahashi, M.T., Fragrance Journal, 21(11), 35 (1993)
2. Kohno, Y.Y., and Yamashita, T.N., Fragrance Journal, 25(4), 29 (1997)
3. Miyazawa, T., Yasuda, K., and Fujimoto, K., Anal. Lett., 20 , 915 (1987)
4. Miyazawa, T., Yukagaku, 38, 800 (1989)
5. Kohno, Y.Y., Sakamoto, O.H., Tomita, K.I., Horii, Y., and Miyazawa, T., Yukagaku, 40, 715 (1991)
6. Kohno, Y.Y., Sakamoto, O.H., Nakamura, T.J., and Miyazawa, T., Yukagaku, 40, 715 (1991)
7. Kohno, Y.Y., Sakamoto, O.H., Takahashi, G.J., and Morosawa, K.J., Keshokaishi, 17, 195 (1993)
8. Kohno, Y.Y., Hagino, A.N., Mori, M., Sakamoto, O.H., and Nakamura, T.J., Shogishi, 27, 33 (1993)
9. Kohno, Y.Y., Egawa, Y., Itoh, S., Nagaoka, S., Takahashi, M. and Mukai, K., Biochim. Biophys. Acta, 1256, 52 (1995)
10. Shindo, L., Witt, E., Han, D., Tzeng, B., Aziz, T., Nguyen, L., and Packer L., Photodermatol. Photo-immunol. Photomed., 10, 183 (1994)

「皮脂抗酸化剤＝チオタウリン」の開発と化粧品への応用

河野 善行

Abstract : Cosmetics and quasi-drugs will play increasingly important roles in our aging and stressful society. We have proposed 3 clinical approaches, anti-drying, anti-UV radiation and anti-oxidation to prevent skin disorders and aging. In this paper, the importance of anti-oxidation mechanisms in particular are discussed. We have discovered that sebum oxidation, which is the starting point of skin oxidation, is triggered by oxidation of squalene. Further research on antioxidant effects of natural ingredients revealed that thiotaurine is effective in preventing squalene oxidation, which leads to the prevention of further propagation of oxidation in the skin. Thiotaurine is known to be compounds involved the metabolism of sulfur containing amino acids in mammals. We have clarified that thiotaurine in skin care products prevents sebum oxidation and consequently prevents skin troubles and skin aging.

Key words : thiotaurine, antioxidant, lipid peroxidation, sebum, singlet oxygen

1．はじめに

資生堂では，「-サクセスフルエイジング- 美しく年を重ねるために」というテーマに89年から取り組んでおり，これが企業文化のバックボーンとなっている。私たち研究開発部門においても得られた成果を商品という形で消費者に還元することでサクセスフルエイジングを具現化しようとしている。

人体最大の臓器である皮膚は，生命体を外界と区別する境界領域に位置し，不断の刺激やストレスに曝されている。これらが長年に渡り繰り返されると，例え個々は小さなものでも皮膚にダメージを蓄積すると考えられている。それゆえヒトの皮膚は「老徴」の現れやすい臓器としてよく認知されており古くからその加齢変化には関心がもたれてきた。皮膚はこのようにセンシティブな臓器であるので，適切なスキンケアが美しく年を重ねる「サクセスフルエイジング」のために必要であると考えられる。

皮膚の変調（肌荒れ，乾燥肌，ニキビ・吹き出物等）や皮膚の老化（シワ，シミ・そばかす，くすみ，柔軟性低下，たるみ，免疫機能低下等）に関与する外部環境よりのストレスは，「乾燥」「紫外線」「酸化」があると考えられている。著者らは皮膚の変調や老化に対応するスキンケアという立場から防御戦略として，「乾燥防御」「紫外線防御」「酸化防御」の重要性を主張し続けてきた（図１）。さらにこれら３つのストレスはそれぞれが密接に関係していることも判ってきた。紫外線は酸化における最も寄与率の高い要因であるし，紫外線は皮膚の乾燥を引き起こす。また酸化

"Development and its application of "Sebum antioxidant thiotaurine" for cosmetics."

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1951年生まれ。1977年３月早稲田大学理工学研究科修士課程修了，同年㈱資生堂研究所入社，1982年新技術開発事業団創造科学推進事業参加，現在㈱資生堂基盤研究センター素材開発研究所 主任研究員，農学博士

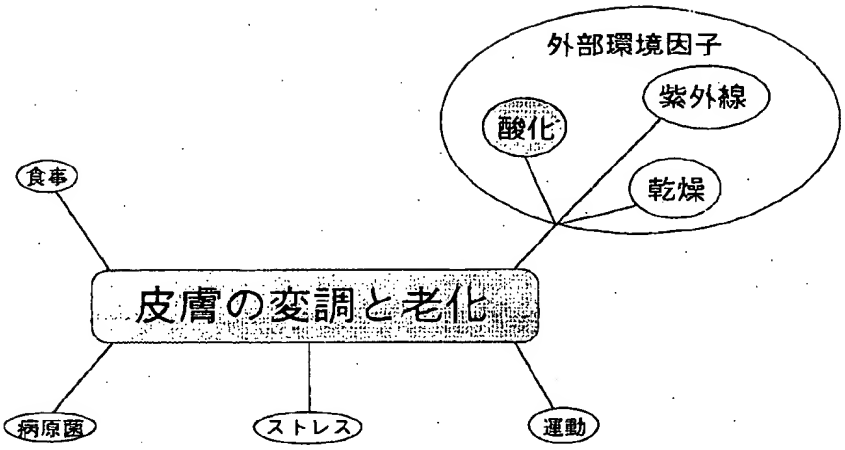

図1　皮膚の変調・老化とその原因

は皮膚の乾燥を引き起こし，乾燥した皮膚は酸化を受けやすい。

本稿では皮膚における「酸化防御」を中心にそれを目的とした素材開発の事例を紹介する。化粧品の配合目的から「酸化防御」を考えてみると化粧品に配合する素材の安定化という目的でのみ「抗酸化剤」が配合されている。化粧品構成成分である薬剤や油分等の酸化安定性を保証することは化粧品の品質保証や安全性の観点より重要であることは自明であるが，今まで化粧品には皮膚成分の酸化防止を明確な配合目的とする素材は開発されていなかった。著者らはそのような素材開発を目的として，皮膚構成脂質の酸化のメカニズムを明らかにし，さらに過酸化反応の生体皮膚に及ぼす影響を明らかにしてきた。また化粧品として「皮膚の酸化」を防御する意味に関しても考察を進めてきた[1,2]。本稿ではそれらも踏まえ，化粧品の目的である肌を健やかに保つために，98年9月発売の「エリクシール」に初めてシリーズ配合した「皮脂抗酸化剤＝チオタウリン」の有用性やその機能についてまとめてみたい。

2．皮膚における酸化

一般に新しい方法論が開発されると，いままで明らかになっていなかった自然界で起こっている現象の理解が進む。そしてその方法論を用いてその現象に対処する効果的な有効成分を探し出すことが可能となり新たな成分や商品の開発に繋がる。

チオタウリンの開発においても，新しい方法論であるCL-HPLCシステム[3,4]が大きく寄与したと考えられる。図2に著者らの一連の研究の端緒となったクロマトグラムを示した。太陽光に暴露した皮膚より採取した皮脂のCL-HPLC分析結果であるが，振り切れたチャートが今までのカテゴリーにない化粧品素材開発のヒントを雄弁に語っている。その後皮膚における酸化では皮脂中のスクアレンが最初のターゲットとなっていること，スクアレンヒドロペルオキシドのスペクトルによる同定，また標品を用いてCL-HPLCシステムが

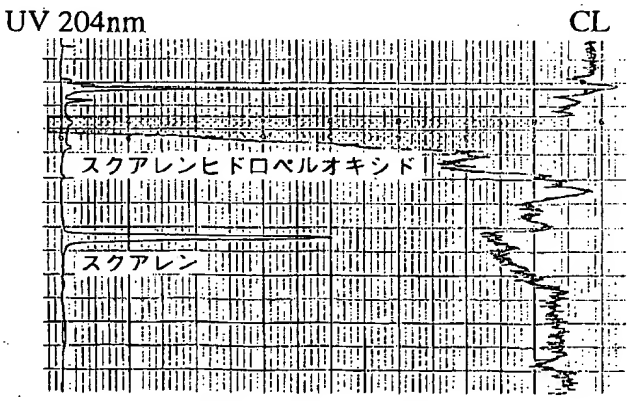

図2　酸化した皮脂
（4月晴れ30分間太陽光照射）

fmol のオーダーにも達する検出感度を有していることも報告してきた[5-7]。さらに皮表における脂質過酸化反応はヒトに照射される紫外線量に伴って増大すること(図3)，ヒト皮表における脂質過酸化反応の加齢変化を観察すると防御システムが完備していない幼年やそれが低下する加齢にともなって過酸化の度合いが増加することも報告してきた(図4)。そして一般生活環境下，種々の酸化ストレスによってヒト皮表で常に生成しているスクアレンヒドロペルオキシドは，細胞傷害性を有していた。また実際の皮膚に近い皮膚再構築系での検討で，スクアレンヒドロペルオキシドから発生するラジカルの酸化伝播反応により皮膚内部のケラチノサイトや線維芽細胞へ傷害を与えることも観察してきた。すなわち皮脂の酸化は皮膚における酸化の始まりであり，単なる皮膚上で起こっている現象に止まらず皮膚内部にも悪影響を及ぼすと考えられる[8]。

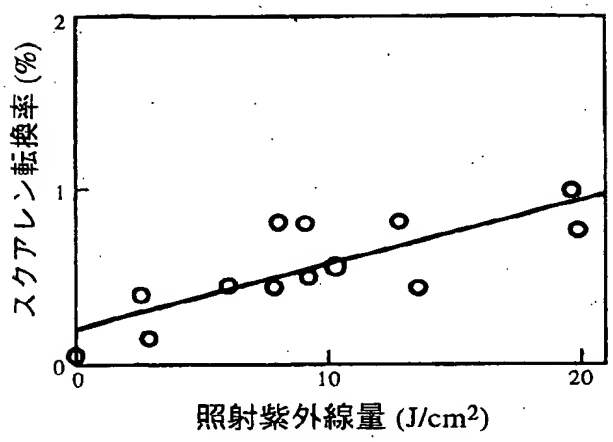

図3　ヒト皮表の脂質過酸化反応
(紫外線照射量の影響)

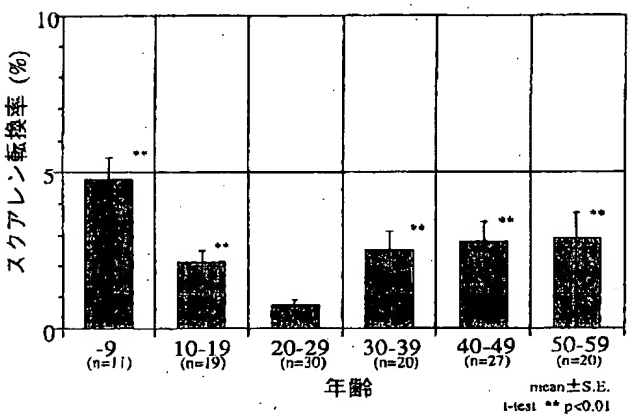

図4　ヒト皮表の脂質過酸化反応
(加齢の影響)

3．皮膚における酸化反応の物理化学的理解

前項で述べてきた現象論に物理化学的考察を加えてきた[9]。皮膚上に存在する脂質類と一重項酸素との反応速度定数を測定するとスクワレンは高い一重項酸素との反応性を有していた（表1）。一重項酸素は健常なヒト皮膚においても一般生活環境下発生していると考えられるが，上述した理由によりスクアレンはヒト皮表において最初の酸化ターゲットとなっているものと考えられる。このことは皮表において一重項酸素がキーとなっている活性酸素種であることを強く示唆する科学的根拠を与えるものでもあった。すなわち皮膚における酸化に対応する化粧品を設計していく上では，一重項酸素に対応することが第一に必要と考えられる。また測定可能なパラメータとして，

表1　脂質類の一重項酸素反応速度定数 (k_Q)

脂質類	化学式	二重結合数	k_Q [$M^{-1}s^{-1}$]
オレイン酸	$C_{17}H_{33}COOH$	1	1.7×10^4
リノール酸	$C_{17}H_{31}COOH$	2	4.2×10^4
リノレン酸	$C_{17}H_{29}COOH$	3	8.0×10^4
アラキドン酸	$C_{19}H_{31}COOH$	4	10.0×10^4
ドコサヘキサエン酸	$C_{21}H_{31}COOH$	6	15.0×10^4
スクアレン	$C_{30}H_{50}$	6	56.2×10^5
コレステロール	$C_{27}H_{46}O$	1	6.7×10^4

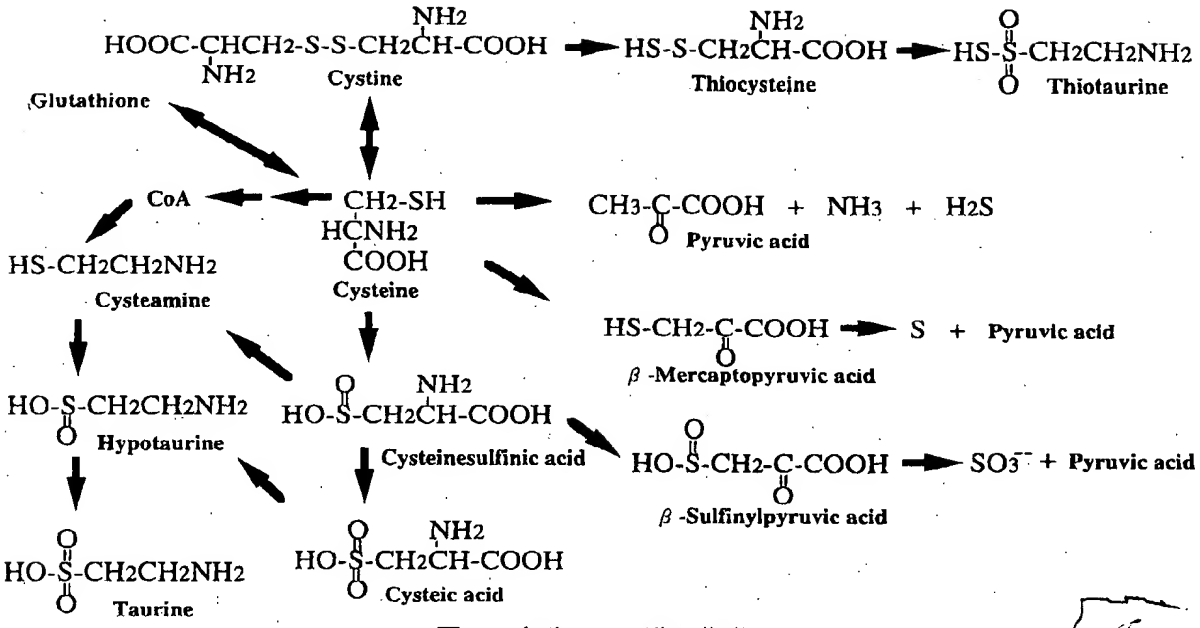

図5　含硫アミノ酸の代謝
A. White, P. Handler, E.L. Smith; Principles of BIOCHEMISRY

皮脂の過酸化の度合いをモニターすることも有用であると考えられた。

4．皮脂抗酸化剤「チオタウリン」の開発

皮膚における酸化を防御し，皮膚を健やかに保つためには，皮膚における酸化の最初のステップである皮脂の酸化を防御することが重要であり具体的には，一重項酸素消去活性の高い物質を皮膚に適用しなくてはならない。しかも単に一重項酸素の消去活性が優れているだけでなく，安全性はもとより，処方への配合のし易さまた安定配合ができること，また商品としてその安定性が保証できること等々が必要条件である。すなわち化粧品素材としてトータルバランスが優れていることが皮膚成分の抗酸化を標榜する化粧品素材の設計や選択においてはなによりも重要なことと考えられる。

上述した観点で種々候補物質をスクリーニングしていったが，我々はその物質を生体成分から選択した。生体皮膚の有しているバランスを保つために酸化ストレスを受け変動し易いチオール化合物を補給し，生体防御システムを補強・再構築することを企図した[10]。著者らが選択したチオタウリンは哺乳類における含硫アミノ酸代謝過程に存在する物質でもある（図5）。またこれらの化合物が眼や生殖器官等の外部よりの酸化ストレスに曝されたりエネルギー消費の多いと考えらるところに比較的多く存在することから，チオタウリンやヒポタウリンが代謝過程で存在する合目的性を議論する報告も見られる。

5．チオタウリンの保湿性

チオタウリンは広義の意味ではアミノ酸の一種とも考えられ，保湿効果のポテンシャルも有していると推定された。著者らは保湿効果を効果の持続性も考慮しヒト皮膚上で検証した（図6）。保湿効果は既に使用されている代表的な保湿剤と比較しても劣らない効果を有していることを確認した。乾燥と酸化は関係することを前述したが「乾燥防御」と「酸化防御」は皮膚を健やかに保つために相乗的に機能することが期待される。

6．チオタウリンの抗酸化性

チオタウリンの一重項酸素反応速度定数を測定し，その結果を表2に示した。化粧品にも用いら

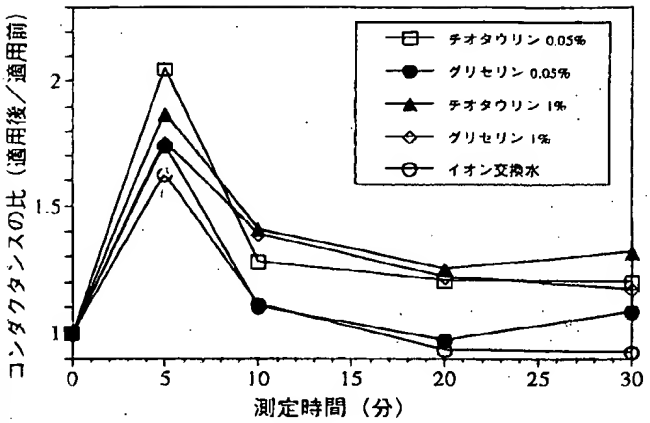

図6　チオタウリンとグリセリンの保湿効果の比較 (n=9)

れている代表的な抗酸化剤と比較しても高い一重項酸素消去活性を有していた。皮脂分泌量から計算されるヒト皮表のスクアレンのモル数また化粧品製剤として皮膚上に適用されるチオタウリンのモル数を考慮し，さらにそれぞれの一重項酸素との反応速度よりヒト皮表で起こっている過酸化反応をどの位防御できるか計算によって求めることが出来る。物理化学的にはチオタウリンの一重項酸素消去活性は十二分に満足のいく値であったので実際のチオタウリン含有のクリームを作成してそれをヒト皮表に塗布してその効果の検証を試みた。具体的には，所定量のチオタウリンを配合したクリームを塗布した部位，また同じ処方でチオタウリンのみを抜去したクリームを塗布した部

表2　抗酸化剤の一重項酸素反応速度定数（k_Q）

抗酸化剤	k_Q [$M^{-1}s^{-1}$]
チオタウリン	2.45×10^{7}
ヒポタウリン	6.97×10^{6}
BHT	4.91×10^{6}
d-α-酢酸トコフェロール	1.60×10^{6}
アスコルビン酸	8.30×10^{6}
スクアレン	5.62×10^{6}

位，なにも塗布しなかった部位それぞれを設け紫外線を照射した。そしてそれぞれの部位より皮脂を採取して CL-HPLC 分析をすることで過酸化されたスクワレンの割合を求め，結果を図7に示した。何も塗布していないブランク部位，チオタウリンを含まないプラセボクリーム塗布部位に比べて，チオタウリンを含有するクリームを塗布した部位の皮脂は統計的有意に酸化が防御されていることを確認した。さらにその効果はチオタウリンの配合濃度に依存していることも合わせて確認した。

7．チオタウリンの安定性

化粧品に配合したチオタウリンの安定性に関しても検討を行った。結果を図8に示したが，チオタウリンは熱（50℃）または光（太陽光曝露）に対しても比較的に安定であることを確認した。抗酸化効果を有する化合物の中では大変

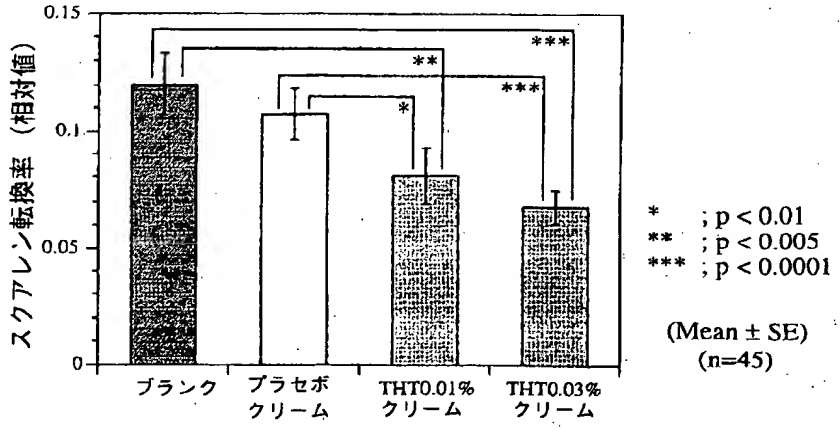

図7　チオタウリンのヒト皮脂酸化防御効果
THT；チオタウリン

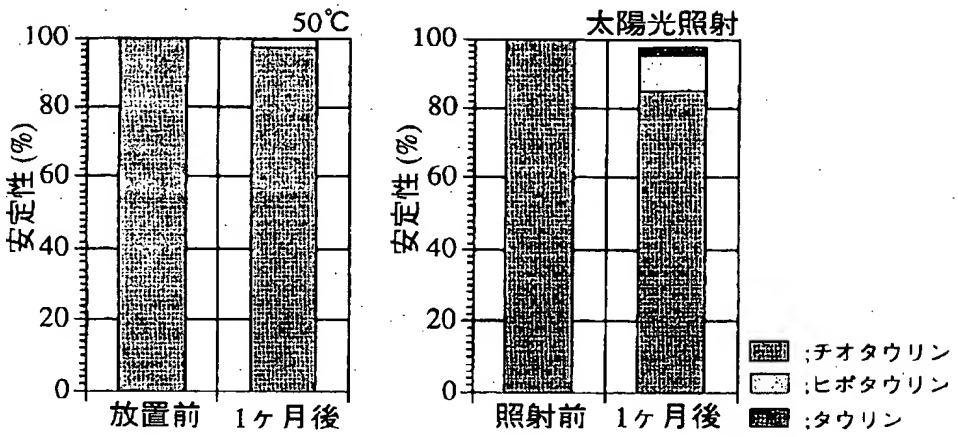

図8　チオタウリンの安定性（pH=6.0）

特異な存在であると考えられる。さらに本品の特長として特記出来ることは，酸化され変化したとしてもその主成分は，すでに化粧品原料として認可されているすなわちその安全性が保証されているヒポタウリンやタウリンとなる点である。化粧品素材としてチオタウリンはトータルバランスに優れている抗酸化素材であることを示す根拠でもある。

8．まとめ

著者らは，化粧品素材として皮脂抗酸化剤＝チオタウリンを開発した。チオタウリンの効果をヒトで検証するとともにその安全性はもとより安定性も優れていることを確認した。すなわちチオタウリンは化粧品用抗酸化素材として総合的に優れたものであった。そしてチオタウリンを配合した化粧品適用の皮膚生理に意味するところは，皮膚における酸化の最初の段階を防御することにあり，ヒトにおけるファーストエイジングともいえる皮脂の酸化を防御するところにある。著者らはそれが美しく年を重ねるために重要であり「サクセスフルエイジング」を具現化するスキンケアの重要な一手段であると確信している。

参考文献

1）河野善行，高橋元次，*Fragrance Journal*, **21**(11), 35 (1993)
2）河野善行，山下豊信，*Fragrance Journal*, **25**(4), 29 (1997)
3）Miyazawa T., Yasuda K., and Fujimoto K., *Anal. Lett.*, **20**, 915 (1987)
4）宮澤陽夫，油化学，**38**, 800 (1989)
5）河野善行，阪本興彦，富田健一，堀井和泉，宮澤陽夫，油化学，**40**, 715 (1991)
6）河野善行，阪本興彦，中村哲治，宮澤陽夫，油化学，**40**, 715 (1991)
7）河野善行，阪本興彦，高橋元次，諸沢敬二，香粧会誌，**17**, 195 (1993)
8）河野善行，萩野滋延，森眞輝，阪本興彦，中村哲治，高橋元次，粧技誌，**27**, 33 (1993)
9）Kohno Y., Egawa Y., Itoh S., Nagaoka S., Takahashi M. and Mukai K., *Biochim. Biophys. Acta*, **1256**, 52 (1995)
10）Shindo Y., Witt E., Han D., Tzeng B., Aziz T., Nguyen L. and Packer L., *Photodermatol. Photo-immunol. Photomed.*, **10**, 183 (1994)